REMARKS

Claims 63-118 were pending in the application at the time the Office Action was mailed. Claims 99-109 and 117 have been withdrawn as being directed to nonelected inventions. Claims 63-98, 110-116, and 118 were rejected. By this amendment, claims 1-97, 110-116, and 118 have been canceled. Claims 98, 100, 101, and 106-109 have been amended. New claims 119-158 have been added. Therefore, claims 98-109, 117, and 119-158 are currently under examination in the application.

Oath/Declaration

According to the Office Action, a new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. A new executed declaration in compliance with 37 CFR 1.67(a) is filed herewith.

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because Figures 8-19 have sequences without SEQ ID NOs. Corrected drawings are filed herewith.

Accordingly, withdrawal of this rejection is respectfully requested.

Sequence Rules Compliance

According to the Office Action, this application fails to comply with the requirements of 37 CFR 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures (the "Notice"). Applicant notes that the Notice was not attached to the Office Action. Nonetheless, the Office Action states that Figures 8-12 and page 34 respectively contain sequences without SEQ ID NOs. Because Figures 8-19 actually contain sequences, Figures 8-19 have been amended herein to include appropriate SEQ ID NOs: Applicant submits that page 34 does not include any sequences which lack a corresponding SEQ ID NO:. In the Amendment filed October 29, 2007, applicant amended paragraph 94 (spanning pages 48 and 49 of the application as filed) to include SEQ ID NOs. Applicant believes no further amendment is

required. Filed herewith is a substitute Sequence Listing that includes those sequences found in the Figures but not in the Sequence Listing filed October 30, 2006. Entry of the substitute Sequence Listing is respectfully requested.

Accordingly, withdrawal of this objection is respectfully requested.

Specification

The abstract of the disclosure was objected to for allegedly including incomplete sentences. The abstract has been amended herein to correct any grammatical errors.

Accordingly, withdrawal of this objection is respectfully requested.

Objections to the Claims

Claims 63, 65, 73, 77, 87 and 92 were objected to for improper grammar and lack of identification of trademarks. Claims 63, 65, 73, 77, 87 and 92 have been canceled.

Accordingly, withdrawal of these objections is respectfully requested.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 75, 80, 94, 95, 107 and 112 were rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the written description requirement. According to the Office Action, these claims recite "not excluding others" where the "others" are not described in the specification. Claims 75, 80, 94, 95 and 112 have been canceled. Claim 107 has been amended to no longer recite "not excluding others".

Claims 87, 89, and 92 were also rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the written description requirement. Claims 87, 89 and 92 have been canceled.

Accordingly, withdrawal of these rejections is respectfully requested.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 63-98, 100, 110-116 and 118 were rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office Action states that the

claims are generally narrative and indefinite, failing to conform with current U.S. practice, and are replete with grammatical and idiomatic errors. Claims 63-97, 110-116, and 118 have been canceled. Claims 98 and 100 have been amended to conform with current U.S. practice.

Claims 63-98, 100, 110-116, and 118 were rejected under 35 U.S.C. 112, second paragraph on various other grounds. Claims 63-97, 110-116, and 118 have been canceled. Claims 98 and 100 have been amended to conform with current U.S. practice.

Accordingly, withdrawal of these rejections is respectfully requested.

Claim Rejections Under 35 U.S.C. § 102

Claims 63-92, 96, 97, 110-116, and 118 were rejected under 35 U.S.C. 102(b) as being anticipated by Nazarenko et al. (U.S. Patent No. 6,117,635). Claims 63-92, 96, 97, 110-116, and 118 have been canceled.

Accordingly, withdrawal of this rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. § 103

Claim 98 was rejected under 35 U.S.C. 103 as being unpatentable over Nazarenko et al. and further in view of Webb et al. (Accession No. M60048, 1993) and Buck et al. (BioTechniques 27:528-536, 1999). According to the Office Action, "[s]ince the claimed primers simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers of the Accession no. M60048 and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations." Applicants submit that the combination of Nazarenko et al., Webb et al., and Buck et al. fails to render claim 98 as amended herein, as well as new claims 119-158, obvious for several reasons. New claim 119 (from which claim 98 depends) recites "[a]n improved method of detection and/or quantification of a nucleic acid target sequence by a nucleic acid amplification reaction comprising: (i) a first oligonucleotide sufficiently complementary to hybridize to a first nucleic acid strand of a target sequence and to act as a nucleic acid amplification primer, and a second oligonucleotide sufficiently complementary to hybridize to the complement of the said first nucleic acid strand and to act as a nucleic acid amplification

primer in an appropriate reaction mixture containing the said sample and a polymerase or polymerases, where the polymerase or polymerases are selected from DNA polymerase, reverse transcriptase, and RNA polymerase, wherein the said eaction mixture is subjected to an initial denaturation followed by repeated cycles of a combination of a denaturation step and at least a selective annealing step, which is further followed by an optional extension step, (ii) the said first and the second oligonucleotide primers do not form any combination in absence of an amplification reaction, wherein the improvement comprises:(ii) the presence of a target sequence in the sample being detected with improved sensitivity and specificity of the amplification product through the generation of a signal mainly on formation of a combination of the two primers and a combination of the two labels on the two separate primers on target amplification, and illuminating the amplification reaction mixture; (iii) determining an additional specificity of the target detection by subjecting the amplified product to a melting temperature analysis." This method is not disclosed in or even suggested by the combination of Nazarenko et al., Webb et al., and Buck et al.

Accordingly, the present invention cannot be regarded as reached by trial and error and cannot be regarded as obvious to try. Further, there was no reasonable expectation of success of generating the present invention which provides the advantages described below given the teachings of the cited art. Based on the prior art, no person skilled in the art would anticipate or think of using two FRET moiety labelled primers to amplify and detect a target sequence.

In the claimed methods of the present invention, a signal is generated through the formation of a FRET combination between a donor moiety on a first primer and an acceptor moiety on a second primer of an amplification reaction. In the present invention, a hairpin primer is made of the above primer containing the donor moiety, and an acceptor as a quencher for the said donor moiety to quench the emission of the donor in absence of an amplification reaction. In another embodiment, a hairpin primer is made of the primer containing the acceptor moiety and a suitable quencher (an acceptor for which the said acceptor is a donor) for the acceptor to quench the emission of the acceptor in absence of an amplification reaction. And in a further embodiment, both the primers are hairpin primers of the above construction. In the first embodiment, on amplification of a target, the quenching of the donor is removed allowing the donor to emit radiation and the donor to form a FRET combination with the acceptor to allow a sensitized FRET emission from the acceptor. In case

of use of the primer carrying the acceptor as hairpin primer it allows the acceptor to accept the emission of the donor and emit its characteristic sensitized radiation. In case of use of both primer as hairpin FRET primer, on amplification the quenching of the donor as well as that of the acceptor is removed allowing the donor to emit radiation and the acceptor to absorb radiation emitted by the donor and the donor and the acceptor moieties form a FRET combination resulting in a sensitized emission from the acceptor. The purpose of the use of hairpin primer is to reduce the background radiation in the method of the present application and thus to increase the signal to noise ratio, not for any signal generation as used by the prior art, including Nazarenko et al.

The methods claimed herein provide at least three advantages over the prior art. First, the claimed invention solves the primer dimer and non-specific amplification problems. Second, little optimization of the reaction conditions is required. Third, the invention provides for highly specific detection of a target sequence with three levels of specificity, and a higher level of sensitivity is achieved as a result.

The teachings of Nazarenko et al. would not lead one of skill in the art to use two labelled primers for target amplification. In contrast to the teachings of Nazarenko et al., Applicants discovered that if two amplification primers are used to amplify a short amplification product close to the size of primer dimer, i.e., less than 100 base pair long target sequence, the yield of the amplification product is thirty to forty times higher than a bigger 200 - 400 base pair long amplification product, and no non-specific amplification product or primer dimer is formed. Prior to this, conventional methods involved amplifying a bigger product of the size more than 100 base pairs, and very often more than 200 base pairs for the detection of a target sequence. Amplification of an amplification product in the size range of primer dimer has so far been avoided and even now it is avoided if there is no specific requirement or compulsion. The above finding of higher yield lead Applicants to think of using two fluorophore labelled oligonucleotide primers for monitoring nucleic acid amplification reaction and detection / quantification of a target sequence in spite of the inefficiency of amplification associated to such use of labelled primers.

Nazarenko et al. does not disclose or suggest the claimed invention. Instead, Nazarenko et al. discloses three different ways of detecting a target nucleic acid. The main disclosure of this method is a universal hairpin oligonucleotide that can be used as a primer in an amplification

reaction, which is also provided labeled with a donor and an acceptor MET/ FRET moiety near its two ends. The method discloses the use of a hairpin primer in nucleic acid amplification and a signal generation through the separation of the donor and the acceptor moieties during the amplification reaction. The donor and the acceptor moieties remain close to each other in absence of an amplification reaction. This mode of target detection requires only two primers. Either one of the two primers can be provided as hairpin dual labeled primer and the other primer unlabeled, or both the primers can be provided as hairpin dual labeled primer. In the second case signal will be doubled. There is no interaction between the moieties on one primer with the moieties on another primer. The opening of the hairpin primer during amplification product formation is sluggish and has background problems from non-specific as well as primer dimer product formation. Because of these problems, this method has not been commercially exploited.

Another disadvantage of the methods disclosed in Nazarenko et al. is the inhibition of the amplification reaction. It has been known in the art that inhibition in an amplification reaction results in the formation of more primer dimer, which in turn results in amplification reaction failure. An inhibited reaction will bring down the sensitivity of detection. There are additional disadvantages in this method, e.g., an additional ligation step. This additional step and lower temperature of extension used for the reaction slows down the amplification process further, which in turn increases the chance of formation of primer dimer and non-specific amplification product. This method has still an additional disadvantage. Before a signal is measured, all the unused duplexes of labeled primer and label complimentary oligonucleotide (blocking oligonucleotide) need to be separated or degraded in a separate additional step. A less efficient separation or degradation will result in target detection error. Further, the absolute quantification of a target sequence cannot be carried out; it is only suitable for end point detection.

Further, it is known in the art that an internal label in an oligonucleotide reduces the Tm of the oligonucleotide by 10 – 12 degrees centrigrade. Hence, use of a primer labeled internally requires use of a lower annealing temperature and a labelled primer is not as efficient as an unlabeled primer in an amplification reaction. The requirement of MET/FRET is that the two moieties of a MET/FRET pair should be close enough as signal drops at a very high rate with an increase of distance between the two moieties. And employment of a primer labelled internally with two labels close to each other will reduce the annealing temperature of the primer to a large

extent and will make the amplification reaction extremely inefficient. Use of lower annealing temperature and inefficient reaction will create increased non-specific amplification product and primer dimer problem. And use of two such labeled primers labeled internally with two labels will not result in any target amplification. Further, before a signal is measured all the unused dual labeled primers need to be degraded by an exonuclease enzyme in a separate additional step. A less efficient degradation will result in target detection error. The absolute quantification of a target sequence cannot be carried out; it is only suitable for end point detection.

The claimed invention differs from the teachings of Nazarenko et al. in several ways. A significant difference is that in the methods described in Nazarenko et al., signal generation is based on separation of FRET, while in the present application the signal generation is through formation of FRET. Additional differences are described below.

The Office Action refers to column 16 lines 23 – 26 of Nazarenko et al., which describes a hairpin primer labeled with a donor and an acceptor. The hairpin primer in the disclosure of Nazarenko et al. is labeled with a donor moiety and an acceptor moiety in the duplex stem structure of the hairpin. There is MET / FRET between the donor and the acceptor moieties when the primer is not incorporated in the amplification product and a signal for the detection of a target sequence is generated on removal of the FRET between the two moieties as a result of the amplification reaction. Use of this type of signal generation is also not unique to this method. In this method primers are provided with a donor moiety and an acceptor moiety in a FRET relation in absence of amplification, and a signal is generated from the separation of the two moieties. In contrast, in the methods of nucleic acid detection of the present invention, the two primers are provided labeled separately with a donor or an acceptor moiety and the donor and the acceptor moieties are not in a FRET relationship with each other in absence of amplification. A FRET relationship is formed between the two moieties after the amplification reaction and a FRET signal is generated as a result of the formation of the FRET combination of the two moieties on two primers. In the claimed methods of the present application, signal is not generated by removal of FRET, rather by formation of FRET. The prior art does not teach or suggest generating a signal in this way.

In the claimed invention, primers, when employed in hairpin configuration and labeled with a donor and an acceptor moiety, are not used for generation of a signal through the separation of the donor-acceptor MET/FRET moieties, rather they are used for the reduction of the background

emission from the donor moiety in the emission region of the acceptor and the background emission from the acceptor due to partial excitation of the acceptor by the donor specific excitation radiation. The signal is generated by formation of MET / FRET through combination of the donor and the acceptor moieties on two separate primers and signal is measured by exciting the donor and measuring the sensitized emission from the acceptor moiety.

Further, in the method of Nazarenko et al., when both the primers are used as labeled primer, both the primers are the same hairpin dual labeled primers labeled with the same donor acceptor moieties in FRET relation; on amplification both donor –acceptor moieties get separated generating a double amount of signal. But there is no interaction between the donor-acceptor moieties on two different primers, another difference between the claimed invention and Nazarenko et al. In case of the primer labelled internally with a donor as well as an acceptor FRET moiety though both the primers of the amplification reaction can be used as labeled primers but the efficiency of the amplification reaction would be so low due to poor hybridization of the two primers to the target sequence that there would practically not be any amplification reaction.

In the present invention, the donor and the acceptor moities are on the two amplification primers which do not carry any complementarity between them to form a hybrid. Hence there is no FRET between the donor and the acceptor moieties before the amplification reaction. There is a FRET between the donor and the acceptor moieties after the amplification reaction, yet another difference between the claimed invention and Nazarenko et al.

The Office Action also refers to Example 10 of Nazarenko et al., in which the inventors have described the use of a hairpin primer in amplification refractory mutation system by an allelic PCR and have described the hairpin primer used for the specific mutation detection. The distance of 18 nucleotides is between the 5' end and the 3' end of the said hairpin primer in its closed hairpin configuration. This 18-nucleotide long sequence (actually 20 nucleotide sequence as given in table 5) is the target complimentary sequence of the said hairpin primer. This part of sequence of the hairpin primer hybridizes to the target sequence for extension by the polymerase during the amplification reaction and it is the actual primer sequence. Hence this sequence has to be of the size of a primer, the size of a primer is normally 10 – 30 bases and hence the sequence used is within this size range. The distance of 18 / 20 nucleotides is between the 5' and 3' ends of a single hairpin primer in its closed duplex configuration before the amplification reaction. In the

present invention, the distance of 0 – 25 nucleotides is between the 3' ends of two primers in the amplification reaction, and is not disclosed or suggested in Nazarenko et al.

In the present application two primers labeled separately with a donor and an acceptor moiety are used in a nested PCR and on amplification a signal is generated on formation of a FRET combination of the two moieties, which otherwise remain separated before the amplification reaction. And no additional oligonucleotide is used. Hence the claims are different from the teachings of Nazarenko et al.

Regarding the reference to Figure 7 of Nazarenko et al. in the Office Action, the present inventive methods, in contrast, require only two oligonucleotides, two labels, one on each oligonucleotide, no third oligonucleotide, not many labelings, no separation step or additional enzymatic step, and a positive signal is generated on amplification. The method of Figure 7 of Nazarenko et al. has additional drawbacks and is less efficient. In the method of the present application, the donor and the acceptor moieties on the two primers are separated from each other before the amplification reaction and as the reaction progresses the two moieties come together within the MET distance and genearate a FRET signal, which can be continuously monitored for a target quantitation. In addition, end point detection can also be carried out. The claimed methods are not disclosed or suggested in Nazarenko et al., and provide solutions to the prior art problems.

In contrast to the teachings of Webb et al., the pending claims recite a primer pair combination, e.g., the combination of SEQ ID No 19 and SEQ ID No 25 with the labels and not the gene sequence. This is a specific combination of the two label primers with a distance relationship between the ends of the two primers. In Buck et al., the authors have described the performance of DNA sequencing primers. Requirements for the selection of amplification primers is much more stringent than the requirements for the selection of sequencing primers. Sequencing primers are used with a small stretch of purified nucleic acid while amplification primers are employed in complex and million times bigger and complex genomic samples. Certain stretches of a DNA may not provide for any good amplification primers, even if they provide for a number of good sequencing primers.

Nucleic acid target detection by nucleic acid amplification is a highly sensitive method as the same provides a very high level of amplification. In such a high level of amplification a lot of

non-specific amplification products are also formed. Hence the problem of such a method of high sensitivity is specificity. And specificity has been a major concern in this field and next concern has been sensitivity. Another problem related to specificity is formation of primer dimer, which is a dimer of primers. The formation of primer dimer reduces the sensitivity, at times resulting in failure of the amplification reaction. Actually there are two classes of nucleic acid amplifications methods, one is through use of only two primers, and the second class is through use of a probe in addition to the two primers. The majority of the methods are of the second category. Use of two primers alone is a general method, it does not ensure specificity, for specificity it requires further steps like separation on a gel or determination of melting temperature of the amplification product in addition to a great deal of optimization of amplification reaction; where as in probe based method probe hybridizes only to the amplification product which is specific. The probe being specific for a target gives specificity to the amplification. But use of probe slows down the amplification reaction and makes the amplification less efficient. In addition for probe annealing, an annealing temperature less than the optimum annealing temperature needs to be employed. Another requirement of the field has been the absolute quantification of the target and for that MET and FRET has been used. The disclosure of Nazarenko et al. does not provide a solution to the specificity problem as well as primer dimer formation problem, thus requiring a lot of optimizations. Though employment of stringency of annealing may improve the non-specificity problem, avoiding primer dimer formation requires a lot more optimization to find the correct annealing temperature for the same as an annealing temperature below or above the optimum one result in primer dimer formation. Further, they do not offer melting temperature analysis. In contrast, the claimed invention provides a method where these two problems are addressed. Further, the claimed invention provides high specificity (three level of specificity) without requiring any additional oligonucleotide as a sequence specific probe, and does not require any additional oligonucleotide as a blocking oligonucleotide.

The method of Nazarenko et al. has many drawbacks. In case of donor and acceptor FRET moiety labelled hairpin primer the opening of the hairpin primer for amplification product formation is sluggish, which makes the amplification process inefficient and reduces the sensitivity of detection. Further, inhibition due to sluggish opening of the hairpin the 3' protruding sequence of the hairpin primer will form primer dimer with itself or the other primer

resulting in high noise signal and also failure of the amplification reaction. In triamplification, use of blocking oligonucleotide inhibits the amplification reaction; there is an additional ligation step and a lower temperature of extension, which slows down the amplification process. Inhibition and slowing down of amplification process results in formation of more primer dimer, which in turn results in amplification reaction failure, and non-specific amplification product formation. Further, a signal is generated before the amplification reaction, and a signal is measured after all the unused duplexes of labelled primer and labelled complimentary oligonucleotide (blocking oligonucleotide) have been separated or degraded in a separate additional step at the end of the amplification reaction. The reduced signal (not any increase in signal) is the measure of the amplification reaction. A less efficient separation or degradation will result in target detection error. Further an absolute quantification of a target sequence cannot be carried out; it is only suitable for end point detection. The methods disclosed in Nazarenko et al. are cumbersome and time-consuming amplification processes.

The claimed methods of the present invention provide specificity of detection in three different ways, one through the configuration of the two primers to amplify a product of small size, another through the use of distance specificity of MET/FRET signal generation, and thirdly through melting curve analysis of the amplified product. Configuration of the primers allows employment of distance requirement of FRET for the specificity of the analysis. Any primer can sit in many sites in a complex nucleic acid sample resulting in many non-specific amplification products if the reaction condition is not extensively optimised. The present method configures two primers very close to each other separated by a distance of 0 - 25 base pairs. For the two primers to sit in right separation will take a much less time for a short target segment in comparison to a bigger target segment as the hybridisation of the primers to the target is a random phenomenon. This makes the reaction more efficient. Again amplification product being very small, the falling off of the polymerase from the template while extending the primer, which is usually another reason for formation of non-specific amplification products and low efficiency of amplification reaction, does not arise in the present method thus resulting in more efficient reaction and absence of non-specific amplification. The amplification of a specific product of the size close to that of a primer dimer will compete out competitive reaction of primer dimer formation resulting in elimination of formation of primer dimer. Improved efficiency of the amplification reaction also means increased sensitivity. As a result

a specific amplification product can be amplified as a single product without much optimization of the reaction condition thus saving much experimentation and time. Shorter amplification products appear to be more tolerant of less than ideal amplification reaction conditions resulting in highly specific amplification even in a less than ideal condition. The amplification reaction is so efficient, and primer dimer and non-specific amplification product are not formed thus resulting in higher specificity in comparison to other methods; the yield of the amplification product is 30 – 40 times higher than the usual yields obtained by other methods. This higher yield in turn gives higher detection sensitivity in comparison to the other methods. This is one of the unique features of the claimed methods, and this feature provides a very good solution to the two major problems of the prior art.

An additional specificity comes from specificity of FRET distance. FRET being limited up to a distance of 100 angstrom, a signal is generated only when the two FRET moiety labelled primers come in right distance as designed for signal generation. The probability of two such labelled primers coming within such a distance due to the formation of non-specific amplification products (other than the specific amplification product) is practically zero. For example, the probability of two primers twenty nucleotides long coming next to each other by chance is $40 / (1/4^{20}) X (1/4^{20})$, which is almost zero. The fixed range of FRET distance, which has been known in the art, has been used in the present method in an elegant manner to add further specificity to the nucleic acid target detection. Formation of primer dimer, which can interfere in signal, is further reduced due to the use of two such labelled primers because polymerase will find it difficult to extend one primer over the other in presence of the dyes.

A third and an additional level of specificity of target detection come from the provision of melting curve analysis of the amplification product. The amplification product is amenable to melting temperature analysis. Melting temperature analysis allows to check further whether a specific amplification product has been amplified or not, or any primer dimmer has formed or not. This method also allows high sensitivity low background detection because of the use of sensitised FRET signal generation for the detection purpose. This is the only method in the entire field of nucleic acid amplification, which provides three levels of specificity of target detection. In all prior art methods solution to the problem of primer dimer has been only through selection of a good primer pair through design and experimentation and a great deal of optimisation.

Whatever good primers are designed or optimisations are carried out primer dimer formation can not be fully avoided; but in the claimed methods of the present invention, selection of the amplification product as such gives a very good solution to the primer dimer formation problem of the prior art, and it is very unique.

Accordingly, the present invention cannot be regarded as reached by trial and error and cannot be regarded as obvious to try. There was no reasonable expectation of success of generating the present invention which provides the above-described advantages given the teachings of the cited art. Based on the prior art, no person skilled in the art would anticipate or think of using two FRET moiety labelled primers to amplify and detect a target sequence.

Based on the foregoing, applicants submit that the cited references do not render the present invention obvious within the meaning of 35 U.S.C. 103. Applicants submit that the references do not suggest modifying their teachings to arrive at applicant's invention.

Accordingly, withdrawal of this rejection is respectfully requested.

Claims 93-95 were rejected under 35 U.S.C. 103(a) as being unpatentable over Nazarenko et al. and further in view of Andersson et al. (U.S. Patent No. 6,210,897) and Chetverin et al. (WO 1993/17126). Claims 93-95 have been canceled.

Accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

The currently pending claims before the examiner are supported throughout the specification and are patentable over the prior art. No new matter has been added. This application is now in full condition for allowance, and such action is respectfully requested.

The Commissioner for Patents and Trademarks is hereby authorized to charge any underpayment of fees or credit any overpayment of fees to Deposit Account No. 50-0951.

The examiner is cordially invited to call the undersigned if clarification is needed on any matter within this amendment, or if the examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

In re Application of: Amirul Islam
Application No.: 10/516,361

Respectfully submitted,

AKERMAN SENTERFITT

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